Ciclo di incontri – Tavolo di discussione

PATCH-CLAMP SINGLE CHANNEL RECORDING AS A TOOL FOR DISSECTING KINETICALLY DISTINCT GATING STATES IN ION CHANNELS

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Using the patch-clamp technique, electrophysiologists have been able to record the ionic fluxes through the pore of single channel proteins, and to clearly distinguish when the channel is functionally closed (i.e. it does not allow the passage of ions) and when it is open (i.e. when ions pass through the channel originating an electrical current that can be recorded). The detailed analysis of these recordings, namely the resulting open and closed dwell time histograms, has shown the existence of a large number of energetically distinct (closed and open) conformational states, whose behavior and connectivity could be well interpreted using discrete Markov models and transition state theory. These studies indicated that ion channels typically have relatively few (one or two) open states, but many closed states.

More recently, the availability of three-dimensional crystallographic structures of ion channels that provide essential clues on the physical determinants of channels conformational transitions and conformational states, and mutagenesis experiments performed under conditions capable to modulate channel gating, suggested the presence of two gating structures and mechanisms: *i*) an intracellular channel domain that undergoes conformational transitions resulting in the opening and closing of the permeation pore; *ii*) a second conformational transition observed to occur more extracellularly, in the selectivity filter of the channel, and to underlie a second form of gating, which likewise resulted in the opening and closing of the channel pore.

Notably, the number of conformational states normally identified in channel gating from crystallographic structures/mutagenesis experiments are largely fewer than the number of energetically distinct conformational states suggested by discrete Markov models. This observation raises the possibility that not all forms of gating originate from conformational transitions of the channel protein.

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